

Attorney Docket No.: RTS-0335
Inventors: Kenneth W. Dobie
Serial No.: 10/006,972
Filing Date: December 4, 2001
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REMARKS

Claims 1, 2 and 4-20 are pending in the instant application. Claims 15-18 have been withdrawn from consideration. Claims 11 and 15-18 have been canceled. Claim 1 has been amended and claims 21-23 have been added. Support for these amendments is found throughout the specification, and especially at Table 1, pages 84-85, and Table 2, pages 87-89. No new matter has been added by these amendments to the claims. Reconsideration is respectfully requested in light of the amendments to the claims and the following remarks.

I. Restriction Requirement

The Restriction Requirement wherein claims 1, 2, 4-14, 19 and 20 were placed into group I while claims 15-18 were placed into Group II has been deemed proper and made Final. Accordingly, Applicant has canceled claims 15-18 without prejudice, reserving the right to file continuing applications on the canceled subject matter.

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II. Rejection of Claims Under 35 U.S.C. 103 (a)

Claims 1, 2, 4-14, 19 and 20 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wiedmer et al. (WO 97/37225 and WO 99/1935), Sims et al. (WO 99/36536), in view of Wiedmer et al. (200), Branch (1998), Monia et al. (U.S. Patent 6,114,517), and Agrawal et al. (2000). The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill modify the teachings of Wiedmer and Sims and Sims et al. to make antisense compounds as claimed, using the teachings of modified antisense compounds as taught by Monia et al. and the size range taught by Branch, while Agrawal et al. teaches the design of antisense oligonucleotides targeting various regions such as the coding region, 5'-UTR and 3'-UTR of a gene. Applicant respectfully traverses this rejection.

At the outset, Applicant has amended the claims to recite that the antisense compounds of the instant invention are ones targeted to a specific nucleobase region within the sequence of human phospholipid scramblase 3 of SEQ ID NO: 3. Support for this amendment to the claims can be found throughout the specification as filed but in particular at pages 63-86 and Table 1. In Table 1, the nucleobase region as claimed is taught as

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being targeted by a variety of specific antisense oligonucleotides (see page 85 in particular).

Wiedmer and Sims (WO 97/37225 and WO 99/19325) disclose preparation of a phospholipid scramblase, a recombinant DNA sequence encoding a phospholipid scramblase protein, and expression vectors used to express the protein. Also disclosed are inhibitors of phospholipid scramblase including monoclonal antibodies, as well as the general idea of using antisense oligonucleotides derived from a DNA sequence encoding a phospholipid scramblase. The patents also teach use of peptides and peptidomimetics to inhibit phospholipid scramblase. Methods of treating various diseases and conditions using the inhibitors are disclosed. Nowhere do these patents, however, teach or suggest the inhibition of phospholipid scramblase of SEQ ID NO: 3 with antisense compounds targeted to a specific nucleobase region of SEQ ID NO: 3. Accordingly, these patents, alone or when combined with other cited art, fail to teach or suggest the limitations of the amended claims.

Sims et al. (WO 99/36536) disclose methods to extend the viability of mammalian cells by inhibiting the expression of a phospholipid scramblase, including use of a phospholipid

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scramblase antisense mRNA molecule, a mutant or truncated form of a phospholipid scramblase such as an alternatively spliced phospholipid scramblase mRNA, a scramblase containing non-conservative substitutions, and by preventing post-translational modifications such as fatty acylation. Also disclosed are methods for diagnosing cancer. Nowhere does this patent teach or suggest the inhibition of phospholipid scramblase of SEQ ID NO: 3 with antisense compounds targeted to a specific nucleobase region of SEQ ID NO: 3. Accordingly, this patent, alone or when combined with other cited art, fails to teach or suggest the limitations of the amended claims.

The secondary references cited fail to overcome the deficiencies in teaching of the primary references when considered alone or when combined.

Wiedmer et al. (2000) disclose the full length cDNA encoding phospholipid scramblase 3 from human erythroleukemia cells. Nowhere does this paper teach or suggest antisense compounds of any type targeted to human phospholipid scramblase 3, including compounds as claimed.

Branch (1998) is a review paper on the technology of antisense. The paper, in fact, discusses the problems with

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antisense technology and the development of drugs based on antisense. Nowhere does this paper teach or suggest antisense compounds of any type targeted to human phospholipid scramblase 3, including compounds as claimed.

Monia et al. (US Patent 6,114,517) disclose antisense to an entirely different gene, not phospholipid scramblase 3. Although the patent teaches the general technology of antisense and modifications that can be made, nowhere does this paper teach or suggest antisense compounds of any type targeted to human phospholipid scramblase 3, including compounds as claimed.

Agrawal and Kandimalla (2000) is another review paper on antisense technology. The paper discusses many of the issues that have hindered development of antisense as therapeutics. Although the paper teaches that general regions of genes can be targeted by antisense, in theory, the paper fails to provide guidance on which regions might be most suitable for particular genes. Further, nowhere does this paper teach or suggest antisense compounds of any type targeted to human phospholipid scramblase 3, including compounds as claimed.

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Accordingly, this combination of art fails to teach or suggest the invention of the amended claims, even when the papers are considered together.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. The teaching of antisense in general and the structure of a gene is not adequate for one of skill to develop antisense compounds that are targeted to very specific regions of a gene. It is only with the specification in hand that one of skill would understand that antisense compounds targeted to a specific nucleobase region within SEQ ID NO: 3 would be successful at inhibiting expression of the human phospholipid scramblase 3 gene. Therefore, the limitations of the claims as now amended, which specify antisense targeted to a specific region of SEQ ID NO: 3, are not taught or suggested by any of the references individually or when combined. Therefore, the

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limitations of the claims as amended clearly are not taught or suggested by the combination of prior art references, nor is any expectation of successful use of such antisense compounds provided by the combination of prior art. Therefore, the cited references, either alone or when combined, cannot render the

instant claimed invention obvious. Withdrawal of this rejection is therefore respectfully requested.

III. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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MESSAGE: Attached is an Amendment Transmittal Letter (in duplicate);
Amendment in Response to Office Action dated December 22, 2003.

URGENT! PLEASE DELIVER IMMEDIATELY UPON RECEIPT. THANK YOU!
